" CARDIAC CHANGES IN HEPATIC CIRRHOSIS"

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CHENNAI

BONAFIDE CERTIFICATE

This is to certify that this dissertation entitled ‘‘CARDIAC CHANGES IN HEPATIC CIRRHOSIS’’ submitted by Dr. K.Balasubramaniyan to the faculty of GeneralMedicine ,The Tamil Nadu Dr.M.G.R.Medical University ,Chennai in partial fulfillment of the requirement for the award of M.D.Degree Branch 1[General Medicine] is a bonafide research work carried out by him under my direct supervision and guidance.

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CONTENTS

INTRODUCTION

Cirrhosis liver, is characterized by diffuse destruction and regeneration of hepatic parenchymal cells leading to deposition of connective tissue with resulting disorganization of the lobular and vascular architecture. Despite the remarkable regenerative capacity of the liver, once hepatic parenchymal reserve is exceeded, clinically overt or decompensated cirrhosis ensues. Portal hypertension develops due to resistance to blood flow through the liver resulting increase in portal venous pressure leading to diversion of blood flow through low resistance portosystemic collaterals thereby bypassing the liver.

Hyperdynamic circulatory state is one of the manifestation of portal hypertension. The splanchnic vasodilatation is an important factor that promotes and maintains the portal hypertensive state. This in turn leads to activation of neurohumoral pathways that stimulate renal sodium retention, expansion of plasma volume and ultimately accumulation of ascitic fluid in persons with cirrhosis.

Expanded plasma volume also contributes to increase in portal blood flow and portal pressure.

The current study was designed to precisely evaluate the cardiovascular system in a group of patients with hepatic cirrhosis based on clinical examination, elctrocardiography, roentgenography and M-Mode 2-dimensional echocardiography.

AIM OF THE STUDY

1.To clinically evaluate patients with hepatic cirrhosis with respect to changes in heart rate, blood pressure, mean arterial pressure, jugular venous pressure and precordial examination.

2. To document the electrical and morphological alterations in the heart in patients with cirrhosis by means of non-invasive investigations like electrocardiography, roentghenography and M-Mode 2-Dimensional echocardiography.

3. To determine the relationship between the cardiac and hemodynamic parameters and the severity and extent of hepatic cirrhosis.

RELATED STUDIES

RELATED STUDIES

Cirrhosis liver reflects irreversible chronic injury to the hepatic parenchyma characterized by extensive fibrosis, in association with the formation of regenerative nodules with resulting disorganization of the lobular and vascular architecture. Decompensated cirrhosis leads to portal hypertension and hepatocellular failure.

Hyperdynamic circulation more directly suggests the presence of portal hypertention and hepatocellular failure. Various studies have been carried our over the years to evaluate the cardiac and hemodynamic changes in cirrhosis of liver.

The studies done include :

1956- Hecker R and Sherlock S showed that blood pressure is low in patients with heptacellular failure and in terminal phase it further reduces renal function.

.1958 – Murray JF; Dawson, A.M and Sherlock – S also reported the presence of increased cardiac output and hyperdynamic circulation in patients with chronic liver disease.

1960 – Platt. D; Kie, F.E; Lubocinski HP; showed that cirrhotics are less liable for atheroma formation than the general population.

1969 – Schaffner, Bull, found Over 50 patients of cirrhosis four had myocardial infarction and two had severe angina.

1973 – Howel Wl, Manion WC ; reviewed 639 cases of cirrhosis at autopsy and found that incidence of myocardial infarction is about a quarter of that among total cases examined without cirrhosis.

1975 - Lunzer MR, Newman SP; Sherlock S; demonstrated impaired cardiovascular responsiveness in liver disease. 1985 – Lenz K, Klein berger G; et al studied the circulatory behaviour in 26 patients with liver insufficiency and demonstrated significant increase in heart rate, stroke volume, cardiac index with decrease in diastolic pressure, and total peripheral resistance.

1986 - Braillon, Gut, Meng . J Gasthepatol, The magnitude of the hemodynamisc changes in the hyperkinetic state also correlates with the severity of cirrhosis by a modified Pugh's classification.

1988 - Shah, ArchIntMed, ascites with cirrhosis may also be associated with pericardial effusion.

1988 – Minuk GY. MacCannel KC; postulated that decreasd hepatic clearance of GABA may play a note in pathophysiology of hypotension in cirrhotics.

1989 – Kristev A, Mitkov D, studied the role of octanioc acid in the development of cardio vascular disorders occurring in some patients with liver disease associated with increased levels of octanoic acid.

1989 – Henricksen J H, Bendtsen F, Sorensen T.A et al demonstrated reduced central blood volume (heart, lungs and central arterial tree) in patients with cirrhosis liver.

1991 - Heikal, Hall, Lunseth, showed 9 percent of patients dying with cirrhosis had hypertensive heart disease.

1993 – Seina Y, Ohki K; et al studied 19 patients with cirrhosis liver and demonstrated decreased cutaneous blood flow in cirrhotic patients due to increase in arteriovenous anastomosis.

1994 – Meng HC, Lin HC et al evaluated 193 patients with cirrhosis liver and demonstrated that the severity of cirrhosis is closely related to the degree of the hyperkinetic circulatory state and portal hypertension.

1994 – Usha Srinivas, Mahadevan V.S et al evaluated 40 cases of cirrhosis liver by M-Mode and Doppler echocardiography.

1996 - Lee SS proposed that the ventricular hypo responsiveness in cirrhotic patients may be due to cirrhotic cardiomyopathy.

2001 – Moller S, Henriksen JH. Cardiovascular dysfunction in cirrhosis. Pathophysiological evidence of a cirrhotic cardiomyopathy. Scand J Gastroenterol 2001, 36 : 785-794.

2002 – Liu H, Song D, Lee SS. Cirrhotic cardiomyopathy, Gastroenterol Clin Biol 2002; 26 : 842 –847.

2005 – Moeper MM, Halank M, Marc C, Hoeffken G, Seyfarth HJ, Schauer J, Niedermeyer J, Winkler J, Bosentan portopulmonary hypertension. Eur Respir J 2005 ; 25 : 502-508.

2006 – Sfner Moller, Jens H Henriksen Cardiomyopathy complications in chronic liver disease.

REVIEW OF LITERATURE

OVER VIEW OF CIRRHOSIS LIVER

Cirrhosis is a pathologically defined entity which is associated with a spectrum of characteristic clinical manifestations. The cardinal pathologic features reflect irreversible chronic injury to the hepatic parenchyma and include extensive fibrosis in association with formation of regenerative nodules (fig;1). These features result from hepatocyte necrosis, collapse of the supporting reticular network with subsequent connective tissue deposition, distortion of the vascular bed, and nodular regeneration of remaining liver parenchyma. Despite the remarkable regenerative capacity of the liver, once the hepatic parenchymal reserve is exceeded, clinically overt or decompensated cirrhosis ensues.

***CLAS*SIFICATION :**

1. *Micro nodular cirrhosis: There is preponderance of parenchymal nodules that are less than 3 mm in diameter. There is involvement of every lobule. The micro nodular liver may represent impaired capacity for regrowth as in alcoholism, malnutrition, old age and anaemia.*

2. *Macro nodular cirrhosis : In this size of the nodules exceed more than 3 mm in diameter. Nodules are highly variable is size and*

normal lobules are found amongst larger nodules. Regeneration is reflected by large cells with large nuclei and by cell plates of varying thickness eg. Post necrotic cirrhosis.

3. *Mixed Cirrhosis : Combination of micro nodules and macro nodules eg. Biliary cirrhosis.*

Most types of cirrhosis may be conveniently classified by a mixture of etiologically and morphologically defined entities as follows.

1. Alcoholic

2. Cryptogenic

3.Post viral or post necrotic

- *Viral hepatitis [Hepatitis B, Non – A, Non – B.*
- *Hepatitis D, hepatitis C, Cytomegalovirus)*
- *Toxoplasmosis*
- *Schistosomiasis*
- *Ecchinococcus*
- *Brucellosis*

4. Inherited and Metabolic disorders :

- *Haemochromatosis*
- *Wilson's disease*
- *Alpha 1 – antitrypsin deficiency*
- *Galactosaemia*
- *Glycogen storage disease*
- *Gaucher's disease*
- *Hereditary fructose intolerance*
- *Hereditary tyrosinemia*
- *Fanconi's syndrome*

5. Drugs and toxins :

- *Methyldopa*
- *Methotrexate*
- *Isoniazid*
- *Perhexilene maleate*
- *Oxyphenisatin*

- *Arsenicals*
- *Oxyphenisatin*
- *Arsenicals*

6. Biliary Cirrhosis :

- *Primary*
- *Secondary*
- *Hepatic venous outflow obstruction :*
- *Budd Chiari Syndrome*
- *Cardiac cirrhosis*
- *Veno occlusive disease*

***8. Miscelleneous** :*

- *Sarcoidosis*
- *Graft Vs Host disease*
- *Chronic inflammatory bowel disease*
- *Cystic fibrosis*
- *Jejunoileal bypass*

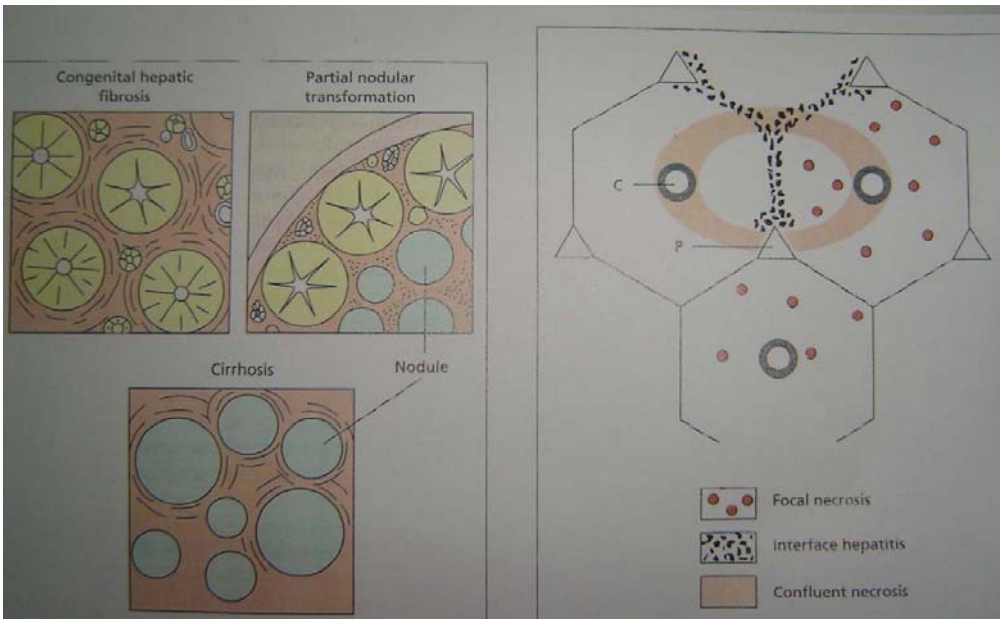
- *Diabetes mellitus*
- *Carcinomatous cirrhosis*
- *Indian childhood cirrhosis*
- *Immunological – Lupoid hepatitis.*

Clinical And Biochemical Classification:

Clinical features of cirrhosis (fig :2) derive from the morphologic alterations and aften reflect the severity of liver damage rather than the etiology of underlying liver disease. Loss of functioning hepatocellular mass may lead to jaundice, edema, coagulopathy, spider telangiectasia, palmar erythema, parotid and lacrimal gland enlargement , nail changes, Duputytren's contractures, gynaecomastia, ascites, testicular atrophy as well as confusion and asterexis suggesting hepatic encephalopathy.

Distorted vasculature leads to portal hypertension. Portal hypertension develops when resistance to blood flow through the liver, is increased and resulting increase in portal venous pressure lead to diversion of blood flow through low resistance portosystemic collaterals thereby bypassing the liver. Hyperdynamic circulation, caput medusae, splenomegaly and gastro esophageal varies more directly suggest the presence of portal hypertention.

Fig.1.FIBROSIS WITH NODULAR REGENERATION



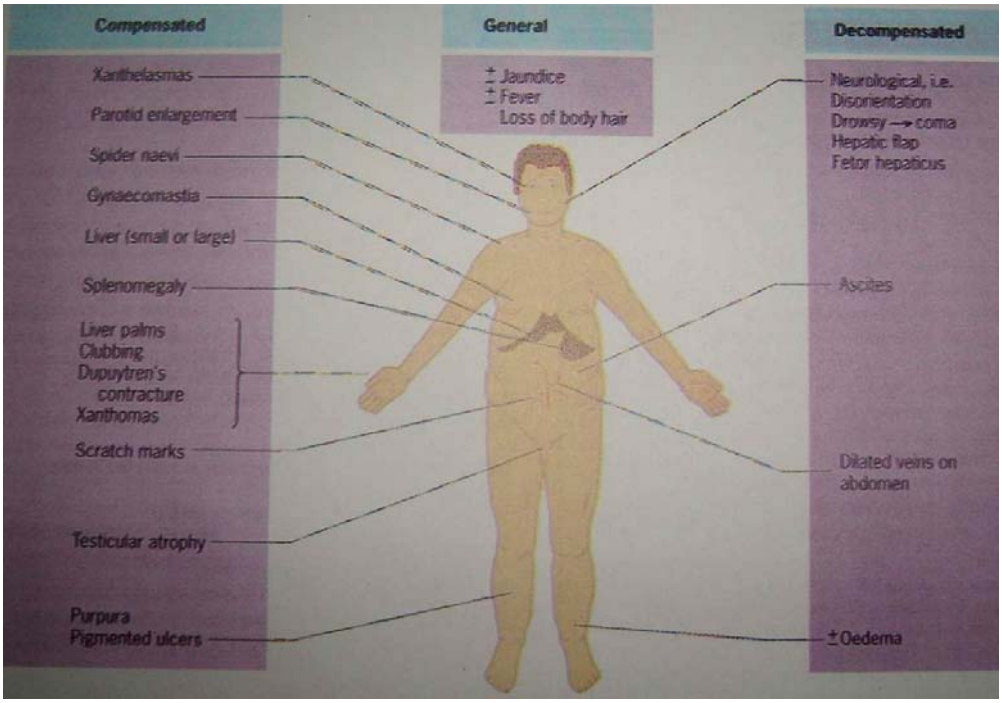


Fig.2.CLINICAL FEATURES OF CIRRHOSIS

Ascites and hepatic encephalopathy result from both hepatocellular insufficiency and portal hypertension.

Compensated Cirrhosis :

This stage is discovered by the following

a) Early symptoms :

- *Vague abdominal pain*
- *Fatigue*
- *Mild pyrexia*
- *Vascular spiders (fig : 3)*
- *Palmar erythema (fig : 4)*
- *Unexplained epistaxis*
- *Ankle oedema*

b) Detected on a routine check up

- *Firm non tender hepatosplenomegaly (fig : 5)*
- *Elevated transaminases*

Fig: 3 VASCULAR SPIDERSAND METHOD OF DEMONSTRAITON

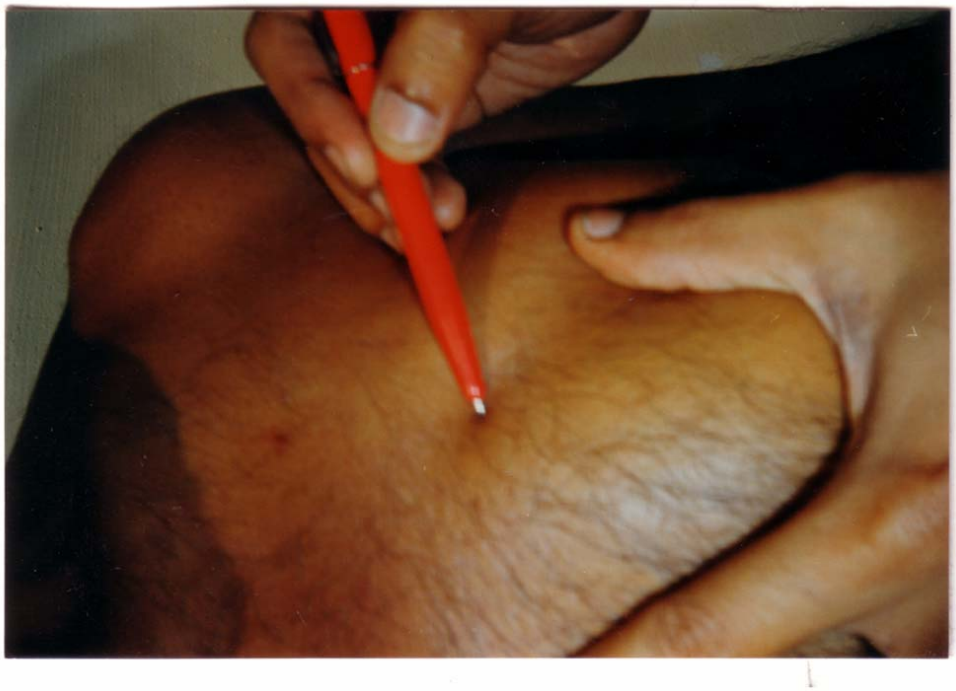


Fig 4 PALMAR ERYTHEMA

c) Background

- *Alcoholism*
- *Hepatitis*
- *Decompensated Cirrhosis*

The patient usually seeks medical advice because of ascites and/or jaundice. Features include poor general health, muscle wasting, weight loss. (fig: 6):Continuous mild fever (37.5 – 38^{0}C) is often due to gram negative bacteremia., to continuing hepatic cell necrosis or to a complicating liver cell carcinoma. Foetor hepaticus may be present. Cirrhosis is the commonest cause of hepatic encephalopathy.

Jaundice(fig : 7) implies that liver cell destruction exceeds the capacity of regeneration and deeper the jaundice, greater the inadequacy of the liver cell function.

The skin may be pigmented. Clubbing of fingers may be present. Purpura over the arms, shoulders and shins may be associated with a low platelet count. Spontaneous bruising and epistaxis reflect a prothrombin deficiency.

The circulation is overactive. The blood pressure is low. Sparse body hair, vascular spiders, palmar erythema, white nails (Leuconychia) and gonadal atrophy are common.

FIG : 5 : SPLENOMEGALY

FIG : 6 : DECOMPENSATED CIRRHOSIS

Ascites is usually preceded by abdominal distention edema of the legs is frequently seen (fig : 8)

The liver may be enlarged and firm or contracted and impalpable. Spleen may be palpable and firm. Hametological manifestations of cirrhosis include anemia, leukopenia and thrombocytopenia which may result from splenomegaly and hypersplenism.

A classification scheme based on a combination of several factors, the Child-Turcotte classification has been useful in estimating long term outcome which is represented below .

CHILD TURCOTTE CLASSIFICATION OF SEVERITY OF CIRRHOSIS

INDEX		***CLASS***	
	A	*B*	*C*
Bilirubin (mg/dl)	*<2.0*	*2.0-3.0*	*>3.0*
Albumin (g/dl)	*>3.5*	*3-3.5*	*<3*
Ascites	*None*	*Easily controlled*	*Poorly Controlled*
Encephalopathy	*None*	*Mild*	*Advanced*
Nutritional Status	*Excellent*	*Good*	*Poor*

FIG : 7 : JAUNDICE

FIG : 8 : ASCITES WITH EDAMA LEGS

PATHOPHYSIOLOGY OF PORTAL HYPERTENSION :

The fundamental hemodynamic abnormality is an increased resistance to portal blood flow. This may be intra hepatic as in cirrhosis or due to obstructed portal vein due to thrombosis. As the portal venous pressure is lowered by the development of collaterals deviating portal blood into systemic veins, the portal hypertention is maintained by increasing the blood flow in the portal system which thus becomes hyperdynamic. Resistance to portal blood flow is exerted along both the hepatic and portal collateral circulation and appears to be modified by vasoactive agents. Portal hypertension is defined as portal venous pressure exceeding 12 mm Hg.

ROLE OF ULTRASOUND:

Ultrasonography has proved to be a useful non invasive and inexpensive method to establish the presence of and aetiology of portal hypertension.

A normal ultrasound shows the liver to have mixed echogenicity. In cirrhosis of the liver the edge of the liver may be irregular and the liver shows coarse echo pattern. It has a fine stippled echogenicity due to increased acoustic attenuation. In end stage cirrhosis the liver is small and very echogenic. It has a nodular border and may be outlined well by ascitic fluid. One portion of the liver may have a different echogenicity from the

FIG : 9 : COLLARERALS OVER THE ANTERIOR ABDOMINAL WALL

remainder and form a bulge. This represents a regenerating nodule. Portal hypertension and splenomegarly are present. Caudate lobe is enlarged relative to the right lobe.

The presence of portal hypertension is sonologically assessed by the following features.

1. *Splenomegaly : If the transducer has a 90^0 angle and the superior and inferior border of the spleen cannot fit on an image, the spleen is enlarged. Static scans are helpful if serial exams for splenomegaly are needed. To evaluate splenic size on a static scan a superior view is preferred. The spleen is enlarged when its anterior border lies in front of the aorta and inferior vena cava and it is at least as thick as a normal kidney.*

2. *Portal vein dilated to >1.3cm. Estimation of portal vein and splenic vein diameter is useful to predict the presence of oesophageal varices. Portal vein and splenic vein size of 12 mm 8 mm are good predictors (93.05% and 94.89% respectively) of oesophageal varices but their size did not differ significantly according to grade of varices.*

3. *Recanalization of paraumbilical veins with in the ligamentum teres.*

4. *Collaterals – Small tortuous vessels at porta hepatis gastric fundus, pancreatic beds splenic hilum – Doppler and colour flow detect vessels.*

5. *Dilated splenic and superior mesenteric veins.*

6. *Ascites*

7. *Normal flow in the portal vein and hepatic artery is in the direction to the liver – Hepatopetal. In severe portal hypertension flow in the portal vein is reversed towards the feet – hepatofugal. Color flow makes this change is direction obvious and Doppler cursor through both vessels simultaneously demonstrates the direction of flow.*

8. *Fenestrated thickened gall bladdar wall is a unique ultrasonagraphic sign seen in patients with portal hypertention. This appearance is possible due to congestive thickness of the gall bladder wall with collaterals in the wall giving it a fenestrated appearance.*

ROLE OF ABDOMINAL PARACENTESIS *:*

Diagnostic paracentesis of about 50 ml is always performed in case of ascites. Complication like bowel perforation and hemorrhage may rarely occures in patients with cirrhosis of liver after paracentesis.

Protein concentration rarely exceeds 2.5 g/100 ml. Higher values suggest infection. If serum albumin to ascites albumin gradient (SAAG) is greater than 1.1 g/dl then it indicates presence of portal hypertension. The SAAG reflects a difference in the oncotic pressures and correlates well with the portal venous pressure.

Fluid usually appears straw coloured or clear and sometimes in advanced cirrhosis chylous ascites may result due to accumulation of chylomicrons on the ascitic fluid.

From 1950 onwards abdominal paracentesis was the accepted treatment of tense ascites. Seleciton criteria for the therapeutic paracentesis include.

- *Tense ascites preferably with edema*
- *Child's grade B*
- *Prothrombin > 40 %*
- *Serum Bilirubin <10 mg/dl*
- *Platelets > 40,000/cu mm*
- *Serum creatinine<3 mg /dl*
- *Urinary sodium>10 mEq/24 hrs*

Usually 5-10 litres of fluid is removed followed by replacement of salt poor albumin 1V 6g/litre of fluid removed. Single large paracentesis of about 10 lts in 1 hour with intravenous salt poor albumin is also equally effective and safe.

ROLE OF LIVER BIOPSY:

Needle Biopsy of The liver :

Needle biopsy of the liver is indicated in the cirrhosis of liver in that it helps to confirm the diagnosis and may provide a clue for the aetiology of cirrhosis. Since the lesions in most cases of cirrhosis liver are diffuse, such a small biopsy specimen is representive of changes in the whole liver.

The exception to this is macro nodular cirrhosis in which aspiration often large nodule may reveal normal architecture. The diagnostic yield may be improved by three consecutive samples obtained by redirecting the biosy needle.

Types of needles used :

- *Vim Silverman Needle*
- *Menghini Needle*

Trucut needle : For the purpose of the study, the trucut needle was chosen because it is of value in cirrhosis patients as it caused less fragmentation.

Biopsty gun (BIOPTER)

Surecut needle : 0.66 mm, May be used to diagnose cirrhosis when the Menghini needle is contraindicated. Risk of complication is minimal.

Approach For liver Biopsy :

1. *Intercostal approach is the most frequent method and it rarely fails.*
2. *Liver biopsy can also be performed via the transjugular route in patient with small liver, failed transcutaneous approach. Wedged and free hepatic venous pressure can be measured simultaneously.*
3. *Direct (Guided) liver Biopsy*
4. *Ultrasound or CT Scan guided liver biopsies give a higher percentage of positivity than the blind percutaneous techniques.*

Contraindications :

- *Coagulation defects*
- *Platelet count less than 80,000/cu mm*
- *Tense ascites*
- *Very small fibrotic liver*
- *Known vascular lesions like hemangioma*

Naked Eye Appearance :

A satisfactory biopsy is 1-4 cms long and weighs 10-50 mg. The cirrhotic liver tends to crumble into fragments of irregular contour.

The biopsy is usually fixed in 10% formal – saline. Routine stains include haematoxylin and eosin and a good stain for connective tissue. Orcein staining is useful to show hepatitis B surface in the hepatocyte; and is also an indicator of cholestasis and Wilson's disease.

Microscopic Appearance :

This is characterized by the following :

- *Parenchymal injury and consequent diffuse fibrosis in the form of delicate bands (portal central, portal-portal, central – central) or broad scars replacing multiple adjacent lobule.*
- *Reorganized vascular architecture.*
- *Parenchymal nodules created by regeneration of hepatocytes.*

PATHOPHYSIOLOGY OF CARDIAC AND CIRCULATORY CHANGES IN CIRRHOSIS LIVER

CHAMBER DYNAMICS AND MYOCARDIAL FUNCTION

Chronic liver diseases like cirrhosis produce high cardiac output states. The mechanisms is uncertain but has been attributed to increased blood volume, intrahepatic arteriovenous shunts, mesenteric arteriovenous shunts and defects in inactivation of circulating vasodilators.

M-Mode 2-Dimenisonal echocardiography is a useful – invasive method of studying the various morphological and functional parameter. In patients with cirrhosis liver prior studies have shown that right ventricular end diastolic volume and right ventricular end systolic volume where significantly reduced in patients whereas left ventricular end diastolic volume and left ventricular end systolic volume and left atrial volume were normal or slightly increased. The right ejection fraction was significantly increased and the left ejection fraction was slightly decreased. Stroke volume was significantly greater. There is also evidence of myocardial contractile function impairment and ventricular hyporesponsiveness to pharmacological or physiological stress. Diastolic dysfunction was found to be 35% in prior studies and more common in alcoholic than in non alcoholics. These changes are reversed following liver transplantation.

Pericardial effusion has been demonstrated in a significant number of patients and is seen as a echo free zone surrounding the heart and if large the whole heart can be seen swinging in to it.

Pulmonary hypertension was seen in 12% of patients.

The incidence of coronary and aortic atheroma is less than the rest of the population. At autopsy, the incidence of myocardial infarction is about a quarter of that among total cases examined without cirrhosis.

HAEMODYNAMIC CHANGES;

Peripheral Vasodilation And Hyperkinetic Systemic Circulation:

Vasodilatation is characteristically shown by flushed extremities, bounding pulses and capillary pulsations.

The cardiac output is raised and this is evidence by resting tachycardia and active precordial impulse and frequent systolic murmur. The splenic blood flow is increased . The renal blood flow especially renal corical perfusion is reduced. Cutaneous micro circulation is reduced due to opening of arterio venous channels and neurohumoral factors. The cardiac index was significantly raised.

The mean arterial pressure and peripheral resistance are markedly reduced. The blood pressure is further lowered and is an ominous sign as it further reduces kidney function. Attempts to raise the circulatory volume

by blood transfusin or drugs such as dopamine are only of temporary benefit.

The systemic vascular peripheral resistance is reduced, as is the arteriovenous oxygen difference. In patients with cirrhosis whole body oxygen consumption is reduced and tissue oxidation is abnormal. This has been related to hyperdynamic circulation and to arterio venous shunting. Thus the vasodilatory state of liver failure may contribute to general tissue hypoxia.

Vasomotor tone is decreased as shown by reduced vasoconstriction in response to exercise, the Valsalva maneuver and tilting from horizontal to vertical posture. Pro bably the increased production of glucagon and other vasodilatory substances in portal hypertension leads to attenuated response to endogenous vasosontrictors which minimizes the systemic effects of activated neurohumoral systems.

The circulatory state is due to the opening up of a large number of normally present but functionally inactive arteriovenous anastomoses that have opened under the influence of a vasodilator substance. The diseased liver might produce such a vasodilator or fail to metabolize one formed else where.

Peripheral vasodilation is thought to play a major role in the activation of neurohumoral systems leading to sodium retention.,

expansion of plasma volume and finally to the accumulation of ascites in patients with cirrhosis. The systemic circulation is therefore markedly vasodilated despite increased levels of endogenous vasoconstrictors because peripheral vasodilation is the stimulus that activates these endogenous vasoactive substances in an attempt to maintain the arterial blood pressure and systemic vascular resistance, there are vascular territories showing marked vasoconstriction such as femoral artery, cubital artery and renal artery. Thus it has been suggested that reversal of splanchnic vasodilation could improve the renal perfusion in patients with cirrhosis, ascites and hepatorenal syndrome.

The nature of the vasodilator remains speculative. The agent responsible for hyperdynamic portal system is probably not the same as that causing systemic hyperdynamic state.

Gamma Amino Butyric Acid (GABA) is a candidate . It is a potent inhibitory neurotransmitter synthesized by the intestinal mucosa and by anaerobic bacteria in the gut. In advanced liver disease hepatic clearance of GABA is impaired and this might cause hypotension by vascular smooth muscle relaxation.

Various gastrointestinal peptides such as VIP, Substance P and CGRP have little effect on the portal circulation Glucagon is a vasodilator and the plasma concentration increases in rats with portal hypertension. Glucagon is a powerful splanchnic vasodilator and it is markedly increased

in cirrhosis. Glucagon increases the azygos flow in patients with cirrhosis but has little effect on cardiac index or haemodynamics so implying little effect on systemic vascular resistance.

Prostaglandins (PGE1, PGE2, and PG12) have vasodilatory actions and prostanoids are released into the portal vein in patients with chronic liver disease. This may play a part in systemic vasodilatation.

In patients with chronic liver disease there is impairment of Kupffer cell function and intrahepatic shunting occurs with impaired clearance of endotoxin resulting in systemic endotoxaemia and bacteraemia. Endotoxaemia will result in activation of macro phages with release of TNF and interleukins whose circulating half life will also be increased in their face of hepatic dysfunction. The elevated levels of endotoxin and cytokines may be important in the development of hemodynamic abnormalities in chronic liver disease with the expression of inducible nitric oxide synthase. High levels of nitric oxide – Endothelium Derived Relaxing Factor (EDRF) results in profound vasodilation. Nitric oxide inhibitors rapidly correct arterial hypotension and reduced systemic resistance.

Recently octanoic acid has been proposed to play a role on the development of cardiovascular disorders. Occuring in some liver diseases associated with high octanoic acid levels in blood serum. Octanoic acid has an inotropic action thereby increasing the cardiac output. It also decrease arterial pressure and vascular resistance. These are inhibited by

indomethacin a fact suggesting that prostaglandin system plays a role in the mechanism of cardiovascular cation s of octanioc acid. This hypothesis represents a new concept regarding the pathogenesis of hyperdynamic cardio vascular syndrome in liver cirrhosis and hepatic encephalopathy.

Table : Circulatory changes in patients with cirrhosis *:*

Increased	*Plasma/total blood volume* *Non-central blood volume Cardiac output* *portal pressure and flow*
Reduced	*Central blood volume* *Arterial blood pressure splanchnic vascular resistance systemic vascular resistance Renal blood flow.*

SPLANCHNIC VASODILATATION AND INCREASED PORTAL VENOUS INFLOW:

Increase portal venous inflow is characteristically observed in advanced stages of p0rtal hypertension. Increased portal blood flow is capable by itself in producing portal hypertension but likely acts to maintain or aggravate portal hypertension in addition to increases resistance. Increased portal venous inflow is the result of a marked arteriolar vasodilation in splanchnic organs draining into portal vein. Many different mechanisms have been suggested t explain the striking haemodynamic abnormality involving neurogenic, humoral and local mechanisms.

Several studies have focussed on the potential role of circulating vasodilators. These vasodilators include neuropeptides, prostacyclin, adenosine, bile acids. Bile acids , ammonia, endotoxin, and a variety of vasodilatory gastrointestinal hormones. Other substances including neuropeptide, secretin, cholecystokinin, pancreatic polypeptide and estrogens may induce splanchnic vasodilation at pharmacological doses but not in the range observed under physiologic conditions.

	Vasodilators	***Vasoconstrictors***
Renal	*Prostaglandin E2* *Nitric oxide* *Kallikrein – kinin system Prostacyclin*	*Endothelin-1* *Thromboxane A2* *Angiotensin II* *Leukotrienes* *Adenosine*
Systemic	*Nitric oxide* *Atrial natruretic peptide* *Adrenomedullin* *Calcitonin gene-related peptide.*	*AngiotensinII* *Noradrenaline* *Antidiuretic hormone* *Neuropeptide Y.*

Glucagon is a powerful splanchnic vasodilator and accounts for 30% to 40% of splanchnic vasodilation of chronic portal hypertension. Glucagon promotes vasodilation by a dual mechanism viz., relaxing the vascular smooth muscle and decreasing the sensitivity to endogeneous vasoconstrictors like norepinephrine, Angiotensin II and Vasopressin.

The endogeneous has also been implicated in splanchnic vasodilation that develops after surgical portocaval shunts.

Studies have demonstrated diurnal variations in portal venous inflow with a maximal increase at night. This probably accounts for the peak incidence of acute variceal bleeding during the night.

The significance of splanchnic vasodilatation and increased portal venous inflow is that most of the pharmacological agents used in the treatment of portal hypertension have been aimed at correcting this factor.

A. Splanchnic vasoconstrictors :

1.Somatostatin and analogues (Octreotide)

2. Beta adrenegic blockers.

3. Vasopressin and analogues (Glypressin) *Propanolol*

Tertatolol

***B. Vasodilators** :*

They reduce vascular resistance in the intrahepatic vasculature.

1. Organic nitrates - Isosorbide di nitrate

Isosorbide 5 mono nitrate

2. Clonidine

3. Calcium channel blocker - Verapamil

Nicardipine

4. Serotonin blockers - Ketanserin

Ritanserin

5. Molsidomine a venodilator -

6. Alpha adrenergic blocker - Prazosin.

C. Miscellaneous :

Reduce blood flow and pressure in gastrooesophagial variceal system

1. *Metoclopromide*
2. *Domperidone*
3. *Pentagastrin*

EXPANDED PLASMA VOLUME :

Increased plasma volume is a constant finding in portal hypertension. It is thought that the expansion of the plasma volume is due to transient sodium retention which in turn is triggered by peripheral vasodilatation. The expanded plasma volume thus represents a response directed to refill the dilated arterial vascular tree. Sequential studies have shown that hypertension, sodium retention and expansion of the plasma volume occur prior to the increase in cardiac output. It is likely that these expanded plasma volume plays a permissive role in the increase of cardiac index.

Recent studies also support the view that the increase in cardiac output in cirrhosis is primarily determined by an increase in the vascular volume and not due to arterial vasodilation.

The expanded blood volume and hyperkinetic circulation allow a hemodynamic stabilization and no further sodium retention occurs. However when the disturbances are more pronounced and accompanied by increased Trans capillary albumin escape it is not possible to achieve such a hemodynamic compensation, and sodium retention continues, leading to the formation of ascites and edema.

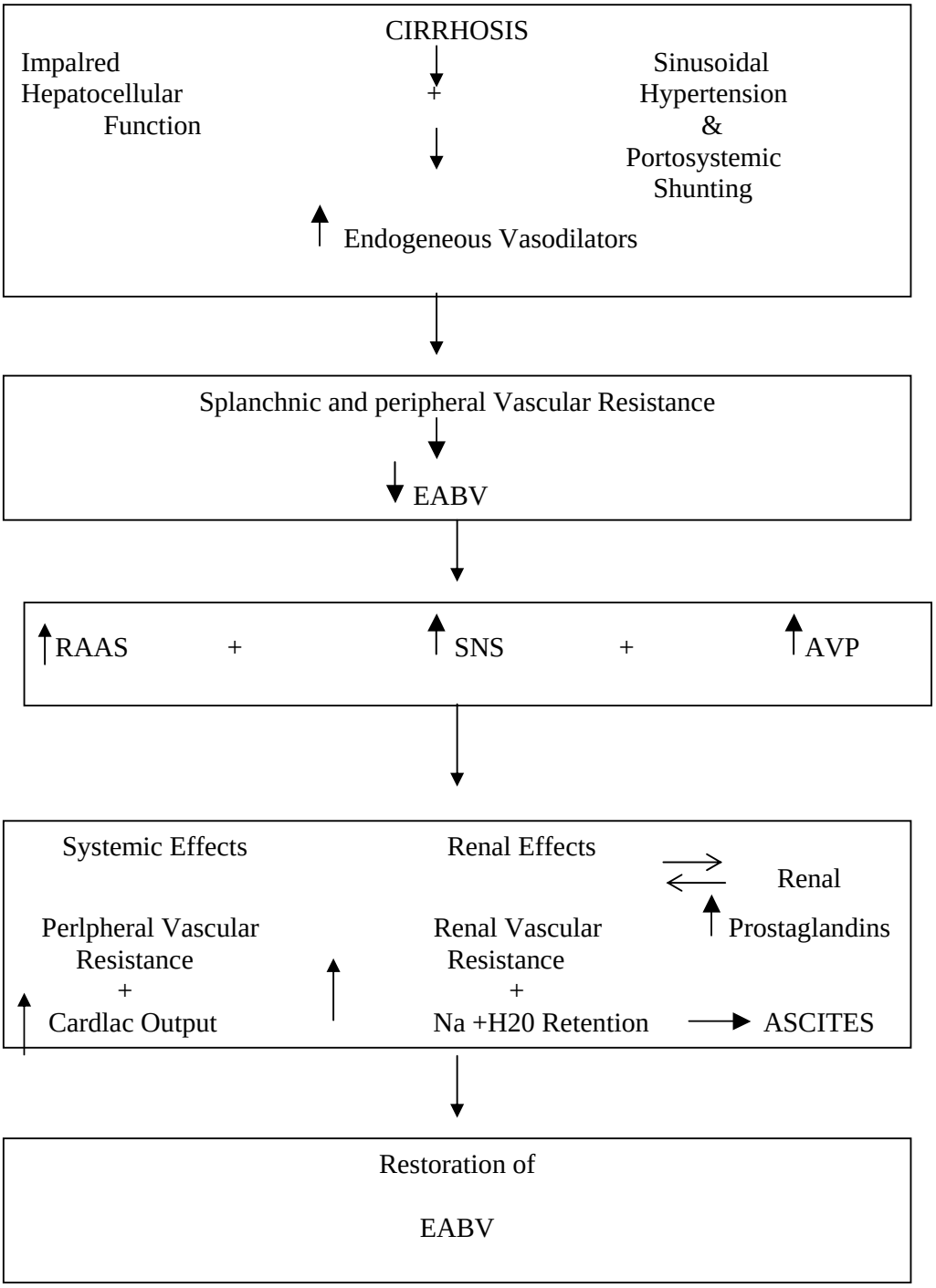
Expansion of plasma volume therefore has a greater importance than what has been traditionally considered in the pathogenesis of circulatory disturbances in portal hypertension. Studies show that the reduction of plasma volume with low sodium and spironolactone represents another possible treatment of portal hypertention. Which could be very appropriate combination therapy with treatments acting through different mechanisms.

SYSTEMIC HEMODYNAMIC FACTORS IN FORMATION OF ASCITES IN CIRRHOSIS LIVER WITH PORTAL HYPERTENSION

Cirrhosis accounts for 80% of cases of ascites. Various theories have been proposed to explain the pathogenesis of ascites of which the most recently proposed theory is as follows :

THE PERIPHERAL ARTERIAL VASODILATATION HYPOTHESIS OF ASCITES FORMATION *:*

More recently, a hypothesis to account for the renal sodium and water retention and ascites formation in cirrhosis has been proposed. This hypothesis has characteristics of both the classical underfill and overflow theories. It suggests that peripheral arterial vasodilatation is the event that initiates sodium and water retention in cirrhosis. Peripheral vasodilatation initially results in a moderate decrease in effective arterial blood volume that stimulates the release of neurohumoral mediators affecting the renal circulation and tubular function and promoting sodium and water retention, thus leading to plasma volume expansion and establishing a new equilibrium with the return of the vasoactive factors to normal levels. As the peripheral vasodilatation becomes more severe, the neurohumorally mediated expansion of plasma volume is no longer adequate to fill the vascular space and the vasoactive control systems become chronically activated. As the liver disease becomes more severe, the abnormalities in the neruohumoral systems



The Perlpheral Arterial Dllatation Hypothesis of Ascites formation in patlents with cirrhosis.
EABV – Effective Arterial Blood Volume SNS : Sumpathetic Nervous System RAAS : Renin –angiotesin – aldosterone system
AVP – Arginine Vasopressin

become more profound and produce extreme change in renal haemodynamics abd tubular function which can lead to the development of the hepatorenal syndrome.

MICROCIRCULATION IN CIRRHOSIS LIVER :

In patients with cirrhosis liver with acute episodes of decompensation there is disturbance of the microcirculation resulting in a tissue oxygen debt that is greater in patients that fail to survive. In such patients the use of prostacyclin, a micro circulatory vasodilator results in an increase in the oxygen uptake with the possibility of lessening or reversing the covert oxygen debt.

CIRRHOTIC CARDIOMYOPATHY :

In cirrhosis cardiac contractile function has been extensively documented to be abnormal. At baseline , cardiac output is increased as a result of hyperdynamic circulation but when challenged by pharmacological or physiological stress ventricular hyporesponsiveness is revealed.

This phenomenon has been termed "Cirrhotic Cardiomyopathy". Diminished myocardial beta adrenergic receptor signal transduction function, possibly caused by a persistent elevation in norepinephrine content has been shown to play an important role. Alteration in cardiac plasma membrane properties due to impaired lipid metabolism is also

crucial. Other possible pathogenic factors proposed include accumulation of cardiodepressant substances caused by hepatocellular insufficiency and ventricular overload secondary to increased blood volume and hyperdynamic circulation. Because the cardiac reserve function is borderline in patients with cirrhosis, cardiovascular status should be carefully monitored, especially when the patients undergo stresses such as live transplantation or portosystemic shunting procedures.

MATERIALS AND METHODS

MATERIALS AND METHODS

The present study was conducted in the Thanjavur Medical College Hospital, between November 2005 and October 2006. 50 patients of cirrhosis liver were selected for the study. These patients were admitted in the general medical wards.

Criteria followed for selection of patients included :

1. *Only patients with clinical, biochemical and sonographic evidence of cirrhosis liver were selected.*
2. *Patients with previously detected heart disease were excluded from the study.*
3. *Patients with inter current illness and those who were critically ill were excluded from the study.*
4. *Patients with cardiac cirrhosis were excluded form the study.*

A detailed history was elicited form the patient with special reference to cardiovascular symptoms. A thorough physical examination was performed in the patients and a special note was made regarding heart rate & rhythm, blood pressure, jugular venous pulse and pressure and precordial examination.

All patients were subjected to routine investigations viz, Blood urea, sugar, complete haemogram, serum cholestrol & liver function tests. All patients were subjected to ultrasound scan abdomen to confirm the diagnosis of cirrhosis. Patients with ascites underwent abdominal paracentesis and fluid was analyzed for protein content and cells. All patients were then subjected to electrocardiography, chest X-ray and M-mode 2-Dimensional echocardiography.

PROFORMA

Cardiac Changes in Cirrhosis

PROFORMA

NAME : AGE SEX M D.O.A

OCCUPATION : I.P.NO F D.O.D

ALCOHOLIC NON-ALCOHOLIC

KNOWN CARDIAC PATIENT YES / NO

COMPLAINTS

ABDOMINAL PAIN ABD MASS JAUNDICE

ABD DISTENTION HAEMATEMESIS

CLINICAL FINDINGS

JAUNDICE HEPATOMEGALY SPLENOMEGALY

PEDAL OEDEMA JVP↑

PULSE : BP : MAP :

INVESTIGATIONS

Hb :
Tc :
Dc :
RBC :
PLATELETS:
PCV :
URINE ALB :
SUG :
DEP :

HBsAG :
Sr. Ceruloplasmin :

Blood Sugar :
Blood Urea :
Serum Creatinine :
Serum Electrolytes : Na+ :
K+ :
LET
Sr Bilirubin :
SGOT :
SGPT :
SAP :
Sr Protein :
Albumin :
Globulin :

Ascitic Fluid Analysis
Glucose :
Protein :

ECG : CXR :

USG ABDOMEN : OGD :

ECHOCARDIOGRAM :

RESULTS

&

OBSERVATION

RESULTS AND OBSERVATION

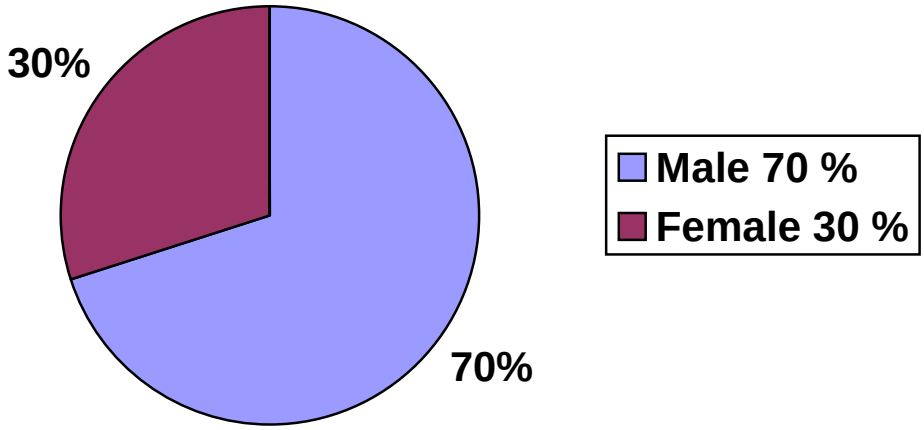


Fig : 9

Out of the 50 patients studied 35 (70%) were males and 15 (30%) were females(fig : 9). The age of the patients ranged from 19 years to 75 years.

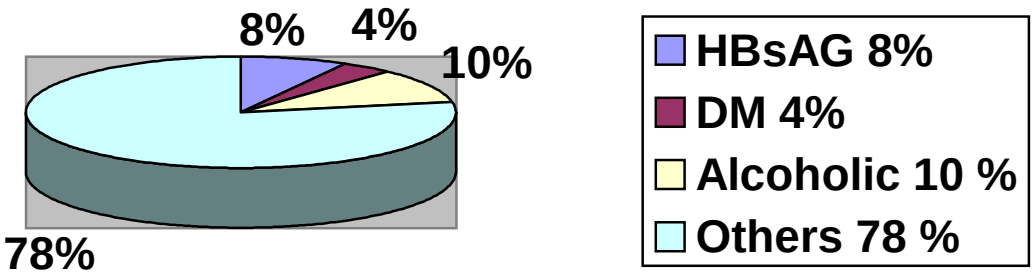


Fig : 10

5 Patients (10%) were alcoholics, 14 patients (28%) had past history of jaundice or, 8 patients (16%) presented with haemetemesis (fig : 11) on admission and 27 patients (54%) had ascites, 9 patients (18%) had jaundice and 6 patients (12%) had clinically detectable splenomegaly on admission. Among this 4 patients were HbsAG+ (8%) and 2 patients were diabetics (4% (fig : 10). All patients had sonographic evidence of cirrhosis.with portal hypertension .

TYPES OF CLINICAL PRESENTATION :

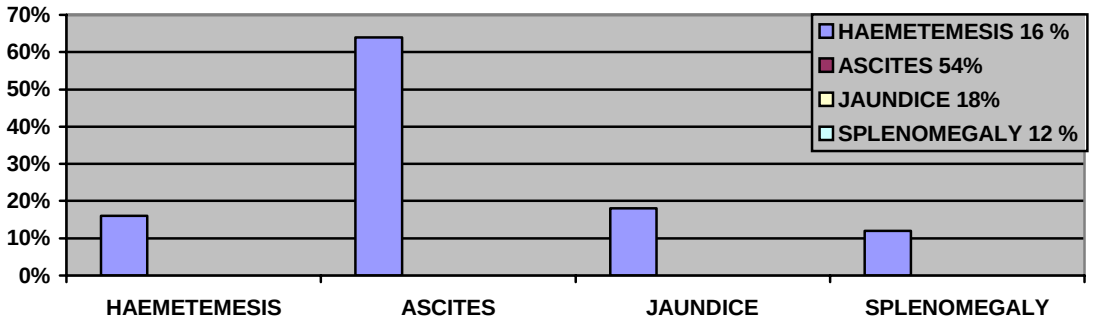


Fig : 11

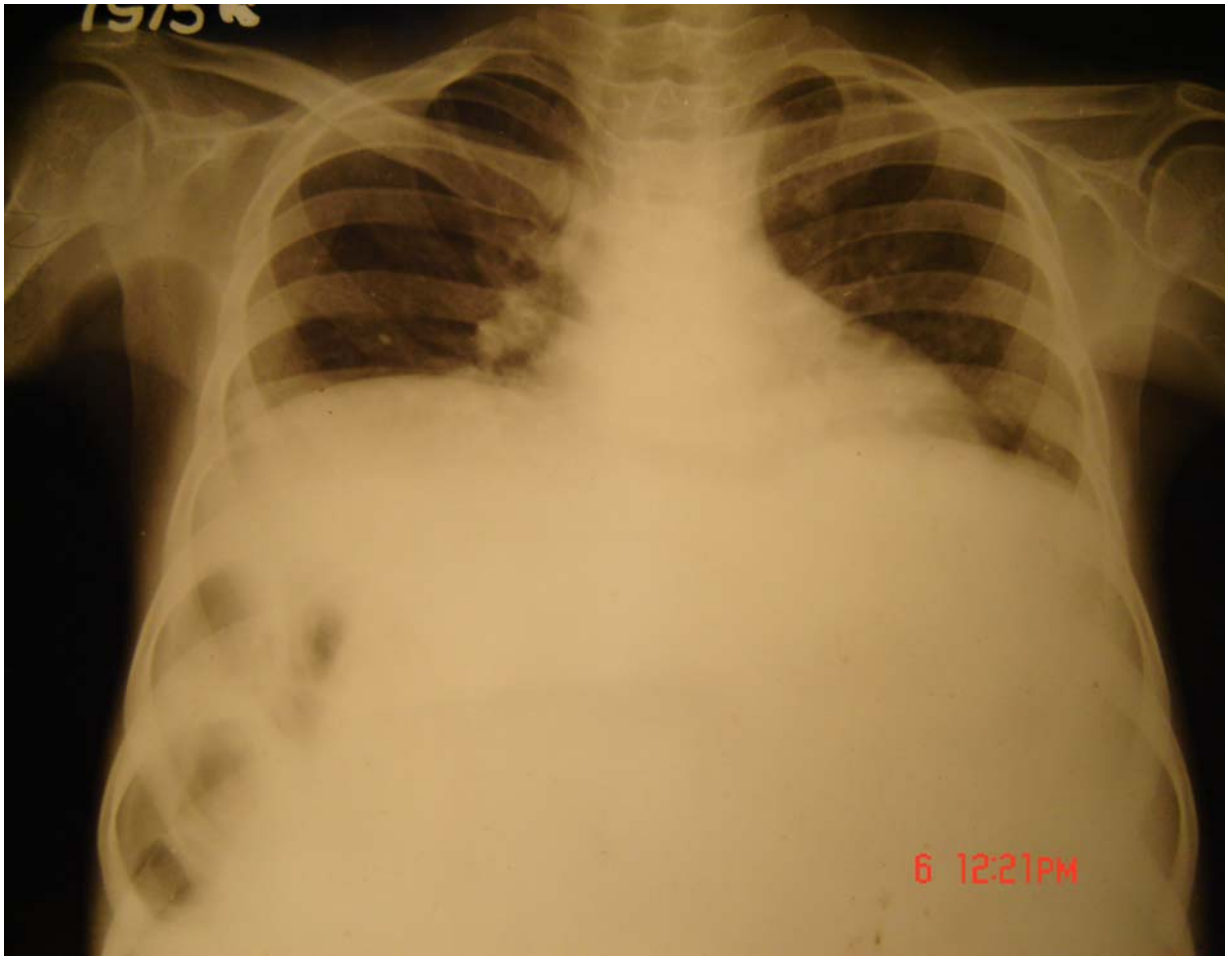
Regarding the cardiovascular examination 20 (40 %) out of 50 patients had symptoms referable to the heart table below :

CARDIOVASCULAR SYMPTOMS AND SIGNS

1. SYMPTOMS PRESINT	*20*	*RANGE*
2. PULSE RATE	*84/ min*	*54 to 120/min*
3. JVP ELEVATION	*12 %*	-
4. BLOOD PRESSURE *SYSTOLIC* *DIASTOLIC* *MAP*	 *110 mmHg* *70 mmHg* *84 mmHg*	 *90 to160 mmHG* *50 to 100 mmHG* *70 to 110 mmHG*
5. HEART MURMURS	*6%*	-
6. CONGESTIVE CARDIAC FAILURE	*6 %*	-

3 Patients (6%) had congestive cardiac failure. The average pulse rate was 84 and it ranged form 54/m to 120/m. The jugular venous pressure was elevated in 6(12%) patients. The systolic blood pressure from ranged 90mmHg to 160 mmHg., the average being 110.mmHg. The diastolic blood pressure ranged from 50mmhg to 100 mmHg ., the average being 70 mmHg. The mean arterial pressure ranged from 70 mmHg to 110 mmHg the average being 86 mmHg Functional high output systolic flow murmur was detected in 3 (6%) patients.

Out of 50 patients 3 patients had elevated blood pressure. Previous studies shows that the systolic blood pressure more than 160mmHG and diastolic blood pressure more than 95 mmHg are the range for hypertension in cirrhorotic patients.



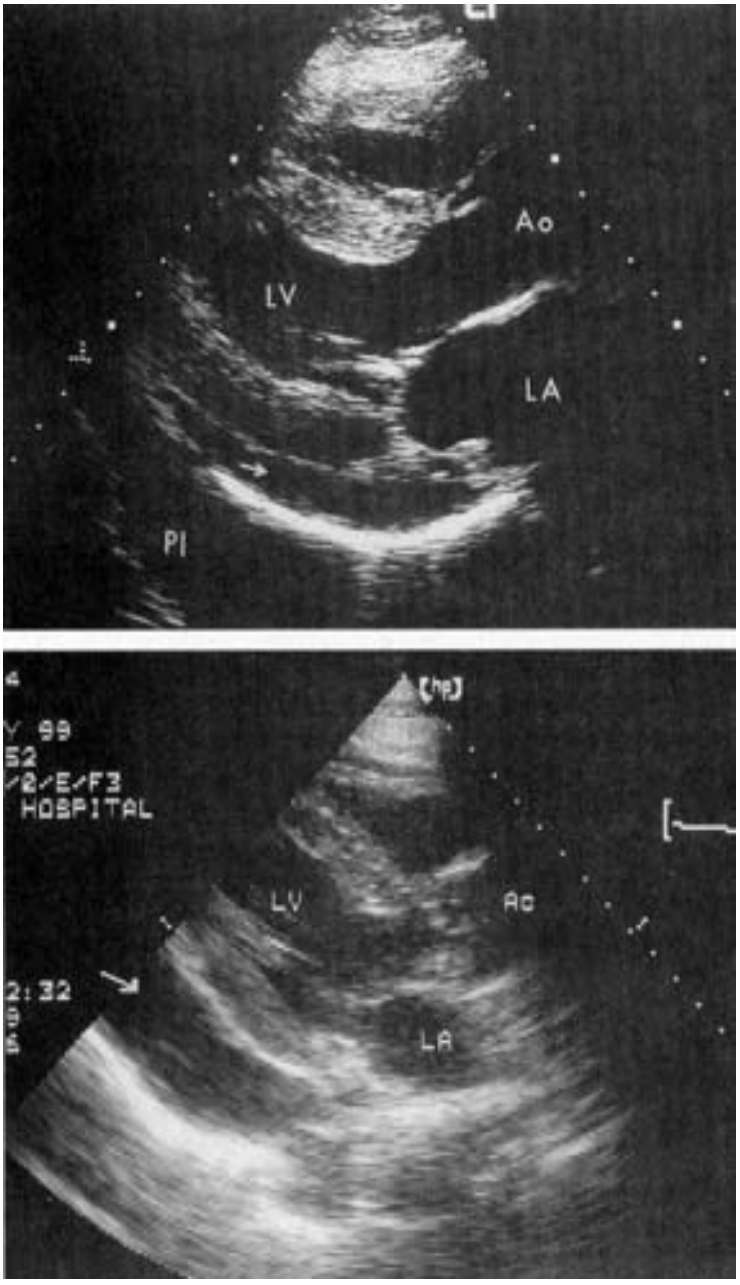
X-RAY CHEST IN ASCITES PATIENT

The electro cardiac gram showed an average heart rate of 82 / m. The low QRS voltage in chest leads and limb leads were found in 10 patients (fig :12). T wave inversion was found in chest leads (V_1 to V_3 / V_6) in 4 (8%) patients, in II, III avf in 7 patiens (14%). Regarding Hemiblock 2 (4%) cases were observed in the study. qs complex in anterior & Inferior leads is seen in 4 patients (8%).

The chest roentgenogram showed Hepatic Hydrothorax in 5 patients (10%). Cardio megaly was evident in chest X – ray in 11 patients (22%) (fig :13).

M-Mode 2 Dimensional Echocardiographic studies , done showed abnormality in 15 (30%) patients. Pericardial effusion (fig : 14) was detected in 4(8%) patients. Regarding enlargement of cardiac chambers – all 4 chambers were enlarged in 3 (6%) patients. With global hypokinesia a nd left ventricular hypertrophy in 1 (2%) patient. One case of porto pulmonary HT was observed in our study (2 %). Akinesia of inferior and anterior wall was seen in 4 (8%) patients (fig : 15) and hyperdynamic flow due to anemia was observed in 2 patients (4 %).

FIG.12.ECHO SHOWS MILD PERICARDIAL EFFUSION



DISCUSSION

DISCUSSION

The aetiology of cirrhosis in patient under study showed a slightly higher incidence of post hepatic or post necrotic cirrhosis as compared to western studies.

With regard to the cardiovascular evaluation, the average heart rate in present study was 84±2 beats per minute. Other studies showed the average heart rate as follows.

Lenz K, Lleinberger G et al 1985 – 101 / min + 2 Vs 78

Bernard M, Rubbloli et al 1991 - 79/min + 2 Vs 71

McCormick P.A; Chin J et al 1995 - 101/min + 2 Vs 78

Present study 2006 - 84±2 / min Vs 74

Thus the present study confirms that there is an increase in heart rate in cirrhosis liver as compared to the average heart rate of healthy subjects, reflecting a hyper dynamic circulatory state.

The average systolic blood pressure, diastolic blood pressure and mean arterial pressure in the present study were 110mm/Hg and 70mm/Hg and 86mmHg respectively. In the other studies they were as follows:

Lenz L; Kleinberger G et al 1985 - Diastolic pressure 56 Vs 71.

McCormick PA, Chin H et al 1995 – 86 - Mean arterial pressure.

The present study shows that the mean arterial pressure is comparable with that of the study done by McCormick P.A et al but the diastolic pressure is within the normal range.

The elevation of jugular venous pulse in 12% of patient reflects an increase in the plasma volume and fluid over load. Significant correlation was demonstrated between the heart rate and mean arterial pressure both of which indicate a hyper dynamic circulation and serum albumin and serum bilirubin levels both of which are indicators of liver dysfunction. The present study clearly demonstrated that hyperdynamic circulation progressively increase with the severity of the liver dysfuntion. The study quoted for this include Meng HG, Lin HC et al 1994 which also concludes that the severity of cirrhosis is closely related to the degree of hyperkinetic circulatory state and portal hypertension. Significant positive correlation was noted between decreased MAP in 36 % and increased HR in 54 %, similarly decreased serum albumin in 32 % and increased serum bilirubin in 44%.

The present study shows that out of 50 patients 3 patients are hypertensive 6 %.

Regarding the electrocardiographic findings not many studies are available showing the various electrocardiographic abnormalities in cirrhosis liver. It has been said that cardiac arrhythmias in cirrhosis liver are always due to a definable precipitating event such as hypo or hyper kalemia, acidosis, hypoxia or cardiac irritation due to insertion of lines, although in older patients the possiblility of ischemic heart disease must not be ignored. One study by Walt, Toyonaga A et al 1995 demonstrated that cardiac arrthythmias is common during surgery, the commonest arrhythmias being premature ventricular contration. The current study shows that low voltage QRS complexes were present in 10 patients. Out of which 4 had pericardial effusion probably reflecting the presence of occult pericardial effusion. T wave inversion was noted in the precordial leads & limb leads in 11 patients and CAHD changes in 4 Patients had no symptoms referable to the cardiac system.

S.NO	*ECG ABNORMALITIES*	*INCIDENCE N=24*	*% 48*
2	*LOW VOLTAGE COMPLEXES*	*10*	*20*
3	*CAHD / INFARCTION* *ISCHEMIC CHANGES*	*4* *10*	*8* *20*

Chest roentgenograms showed that the elevated hemidiaphragms were the commonest abnormality detected and all these patients had ascites and the elevated hemidiaphragms probably reflecting increased intra-abdominal pressure. Cardiomegaly was detected in 11 patients. Hepatic Hydrothorax was found in 5 patients.

***Chest roentgenograms evaluation of patients under study is as follows** :*

X- RAY CHANGES	***INCIDENCE N = 16***	***%***
CARDIOMEGALY	*11*	*22*
HEPATIC - HYDROTHORAX	*5*	*10*

Echocradiographic evaluation of patients under study is as follows :

S.NO	***ECHO ABNORMALITIES***	***INCIDENCE N = 15***	***% 30***
1	*Cardiomyopathy* *Global hypokinesia & chamber enlargement present.*	*3* *(Out of 3, One patients is Alcoholic)*	*6*
2	*Pericardial Effusion*	*4*	*8*
3	*CAHD changes*	*5*	*10*
4	*Porto Pulmonary HT*	*1*	*2*
5	*Hyper dynamic Flow due to anemia*	*2*	*4*
6	*LV Dysfunction (LVEF<49%)*	*3*	*6*

Moderate Anemia < 10 g %, severe Anemia < 7 to 8 gm % (fig : 16)

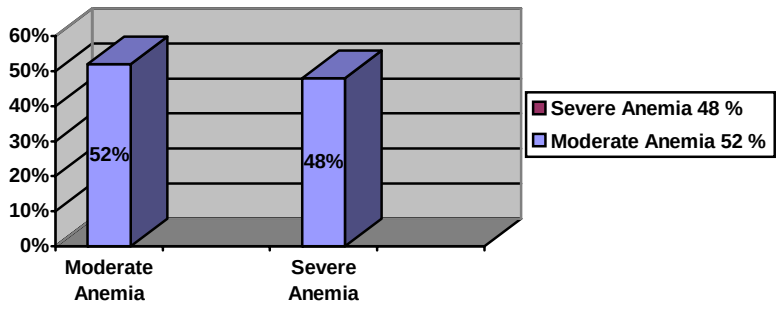


Fig : 16

Current study shows that all the 50 patients were anemic that is < 10 gm %. Among this 24 (48%) Patients were severely anemic and 26 (52%) patients are moderately anemic.

CONCLUSION

CONCLUSION

1. *The result of this study clearly show that large number of patients with hepatic cirrhosis are asymptomatic (40%) with regard to cardiovascular system, have evidence of cardiac involvement in elctrocardiography and echo cardiography.*

2. *cardiac decompensation in cirrhosis is rare despite the high output state and its presence as indicated by left ventricular systolic dysfunction..*

3. *The incidence of hypertension in cirrhosis patients, our study shows 3 patients (6 %).*

4. *Electrocardiographic abnormalities includes low voltage complexes due to pericardial effusion non specific T wave abnormalities and CAHD changes.*

5. *Cardiomyopathy, pericardial effusion, portopulmanary hypertension and CAHD are the Echocardiographic abnor -malities detected in this study.*

6. *All the patients were anemic, either the hyperdynamic circulation and hyperkinetic syndrom is due to cirrhosis or due to anemia is still in controversy. Further it needs a long term follow up and study.*

7. *Cardiac evaluation is a pre-requisite in patients with cirrhosis undergoing stress like surgery because the presence of cardiac involvement adds to the morbidity and mortality.*

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MASTER CHART

(PLEASE VIEW IN NORMAL VIEW)

S. No	Name	Age Sex	I.P.No	HR	Sys BP	Dias BP	MAP	Hb %	Sr. bil	Sr. alb	BLD Urea	USG ABD	
1	Thangaiyan	40/M	912660	64	130	80	96	3.4	0.8	3.4	25	Cirrh / PHT	
2	Mathiyalagan	39/M	911255	98	100	70	80	6	0.1	2.8	37	Cirrh / PHT	
3	Mohammed Arif	74/M	905946	86	140	80	100	8.2	1.4	3	18	Cirrh / PHT	
4	Singaram	75/M	900079	88	120	80	94	6	1.4	4.1	35	Cirrh / PHT	
5.	Rengasamy	60/M	900835	90	100	70	80	4.6	0.8	3.3	22	Cirrh / PHT	
6.	Suresh	19/M	906333	76	110	70	84	9.2	1.6	3	16	Cirrh / PHT	
7	Sanmugam	52/M	889159	84	100	70	80	6.2	6.8	3.5	30	Cirrh / PHT	
8	Thanabal	46/M	908914	78	130	80	96	9	2.4	3	34	Cirrh / PHT	
9	Noornisha	27/F	908856	88	110	70	84	8.8	0.8	3.2	28	Cirrh / PHT	
10	Gandhi	55/M	886274	88	110	70	84	5	1	3.5	15	Cirrh / PHT	
11	Sarbon bee	48/F	889080	80	110	80	90	6.4	2	3.4	22	Cirrh / PHT	
12	Kumar	40/M	891767	88	120	80	94	8.5	1.2	2.5	53	Cirrh / PHT	
13	Baby	59/F	917/05	76	160	100	120	9.4	1	3.7	30	Cirrh / PHT	
14	Arumugam	30/F	882491	90	120	80	94	7.2	4	3	28	Cirrh / PHT	
15	Padma	30/F	884912	76	100	70	80	8	1.4	2.7	16	Cirrh / PHT	
16	Savithiri	58/F	886392	92	110	80	90	7.8	.9	2	39	Cirrh / PHT	
17	Sankar Ganesh	19/M	912983	86	120	70	86	7	1.4	3.4	32	Cirrh / PHT	
18	Indirani	47/F	902192	96	120	80	94	9.2	1	2.3	34	Cirrh / PHT	
19	Sivapakkiam	40/F	910114	88	110	70	83	6.8	1.4	3.3	41	Cirrh / PHT	
20	Govindaraj	50/M	908529	98	120	70	86	8	3.4	2.7	28	Cirrh / PHT	
21	Pandian	48/M	891563	80	180	100	126	10.2	1.8	3.1	34	Cirrh / PHT	
22	Elavarasan	28/M	910963	80	120	80	94	10.4	6	3	24	Cirrh / PHT	
23.	Kathaiyan	40/M	908640	86	100	70	80	7.8	1.2	3.4	36	Cirrh / PHT	
24	Kala	55/F	912876	72	120	80	94	9	.8	3.2	52	Cirrh / PHT	
25	Muniyandi	50/M	876538	84	120	80	94	8	.9	3.2	55	Cirrh / PHT	
26	Arunachalam	45/M	875558	92	110	70	84	8	1.2	3.4	36	Cirrh / PHT	
27	Karuppaiya	49/M	874959	82	110	60	76	9	5.8	3	34	Cirrh / PHT	
28	Sivasubramanian	35/M	871943	74	160	96	113	9.2	1.4	2.8	36	Cirrh / PHT	
29.	Moorthy	39/M	873618	86	100	70	80	5.8	.6	2.6	182	Cirrh /	

												PHT	
30.	Govindaraj	65/M	908531	84	120	80	94	9.2	1.2	2.5	46	Cirrh / PHT	
31	Raman	47/M	873762	80	110	80	90	9.2	1.2	3.2	24	Cirrh / PHT	
32	Thaialnayaki	50/F	876185	80	130	80	96	8.2	1.4	2.7	17	Cirrh / PHT	
33	Uttharasu	45/M	870571	80	110	80	90	5.6	2.6	3	43	Cirrh / PHT	
34	Chandra	40/F	873928	92	110	70	84	8.6	0.8	2.7	21	Cirrh / PHT	
35	Arockia Mary	52/F	822340	80	140	70	84	8	0.8	3.5	33	Cirrh / PHT	
36	Selvamani	50/M	889086	84	110	80	90	4	0.8	2.8	38	Cirrh / PHT	
37	Selvaraj	42/M	878636	80	110	70	84	8.6	1	4	19	Cirrh / PHT	
38	Ragumansha	52/M	875559	98	100	80	86	6.4	1.6	2.8	23	Cirrh / PHT	
39	Rajavarman	51/M	877726	88	110	70	84	9.4	.6	2.3	40	Cirrh / PHT	
40	Gokila	40/F	877437	96	110	80	90	9.8	4	3	21	Cirrh / PHT	
41	Asaraf Nisha	35/F	878448	82	120	80	94	6.2	1.4	2.8	24	Cirrh / PHT	
42	Kaliaperumal	55/M	908750	84	120	80	94	9.2	0.8	3.3	30	Cirrh / PHT	
43	Mani	63/M	879311	88	120	70	86	2.8	.9	3.2	32	Cirrh / PHT	
44	Selvi	35/F	879846	80	110	70	84	7.6	1.2	2.6	94	Cirrh / PHT	
45	Yusuf	39/M	889008	96	110	70	84	7.2	8.2	3.4	18	Cirrh / PHT	
46	Samikannu	65/M	963142	98	120	80	94	6.4	3	2.4	56	Cirrh / PHT	
47	Malarkodi	30/F	884586	84	110	70	83	8.8	0.8	3.5	15	Cirrh / PHT	
48	Addaikklam	65/M	907865	86	110	80	90	9.2	.8	3.0	28	Cirrh / PHT	
49	Dhantayuthpani	53/M	909517	76	130	80	96	8.2	2.8	3.7	42	Cirrh / PHT	
50	Danial	60/M	901250	84	120	80	94	8.6	.8	3.5	36	Cirrh / PHT	